

(12) INTERNATIONAL APPLICATION PUBLISHED UNDER THE PATENT COOPERATION TREATY (PCT)

(19) World Intellectual Property
Organization
International Bureau



(43) International Publication Date
24 February 2005 (24.02.2005)

PCT

(10) International Publication Number
WO 2005/016970 A3

(51) International Patent Classification⁷: **C07K 16/28**,
A61K 39/395, A61P 35/00, C12N 15/13, 15/63, 5/10

(21) International Application Number:
PCT/US2004/013852

(22) International Filing Date: 3 May 2004 (03.05.2004)

(25) Filing Language: English

(26) Publication Language: English

(30) Priority Data:
60/467,177 1 May 2003 (01.05.2003) US

(71) Applicant (for all designated States except US): **IM-CLONE SYSTEMS INCORPORATED** [US/US]; 180 Varick Street, New York, NY 10014 (US).

(72) Inventor; and

(75) Inventor/Applicant (for US only): **LUDWIG, Dale, L.** [US/US]; 14 Lookout Road, Randolph, NJ 07869 (US).

(74) Agents: **SOMERVILLE, Deborah, A. et al.**; Kenyon & Kenyon, One Broadway, New York, NY 10004 (US).

(81) Designated States (unless otherwise indicated, for every kind of national protection available): AE, AG, AL, AM,

AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW.

(84) Designated States (unless otherwise indicated, for every kind of regional protection available): ARIPO (BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW), Eurasian (AM, AZ, BY, KG, KZ, MD, RU, TJ, TM), European (AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR), OAPI (BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG).

Published:

- with international search report
- before the expiration of the time limit for amending the claims and to be republished in the event of receipt of amendments

(88) Date of publication of the international search report:
21 April 2005

For two-letter codes and other abbreviations, refer to the "Guidance Notes on Codes and Abbreviations" appearing at the beginning of each regular issue of the PCT Gazette.

(54) Title: FULLY HUMAN ANTIBODIES DIRECTED AGAINST THE HUMAN INSULIN-LIKE GROWTH FACTOR-1 RECEPTOR

(57) Abstract: This invention relates to human antibodies that bind to human insulin-like growth factor-1 receptor (IGF-IR), to derivatives of these antibodies (Fabs, single chain antibodies, bi-specific antibodies, or fusion proteins), and to uses of the antibodies and derivatives in therapeutic, and diagnostic methods. The invention relates to nucleic acids encoding the anti-IGF-IR, methods of generating the antibodies and expression. The invention further relates to combination therapies using anti-IGF-IR antibodies with anti-neoplastic drugs.

WO 2005/016970 A3

INTERNATIONAL SEARCH REPORT

International Application No

PCT/US2004/013852

A. CLASSIFICATION OF SUBJECT MATTER

IPC 7 C07K16/28 A61K39/395 A61P35/00 C12N15/13 C12N15/63
C12N5/10

According to International Patent Classification (IPC) or to both national classification and IPC

B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)

IPC 7 C07K

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

Electronic data base consulted during the international search (name of data base and, where practical, search terms used)

EPO-Internal, BIOSIS, WPI Data, EMBASE, PAJ, Sequence Search

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category *	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	WO 02/053596 A (PFIZER INC; ABGENIX, INC; COHEN, BRUCE, D; BEEBE, JEAN; MILLER, PENELO) 11 July 2002 (2002-07-11) examples 4,11,12	1-56
E	WO 2004/087756 A (F. HOFFMANN-LA ROCHE AG; GRAUS, YVO; KOPETZKI, ERHARD; KUENKELE, KLAUS) 14 October 2004 (2004-10-14) page 43; example 2	1-56
E	WO 2004/083248 A (PHARMACIA CORPORATION; MORTON, PHILIP, A; ARBUCKLE, J., ALAN; BAILEY,) 30 September 2004 (2004-09-30) examples 3,4	1-56
	-/--	

☒ Further documents are listed in the continuation of box C.☒ Patent family members are listed in annex.

* Special categories of cited documents:

- *A* document defining the general state of the art which is not considered to be of particular relevance
- *E* earlier document but published on or after the international filing date
- *L* document which may throw doubts on priority claim(s) or which is cited to establish the publication date of another citation or other special reason (as specified)
- *O* document referring to an oral disclosure, use, exhibition or other means
- *P* document published prior to the international filing date but later than the priority date claimed

T later document published after the international filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the invention

X document of particular relevance; the claimed invention cannot be considered novel or cannot be considered to involve an inventive step when the document is taken alone

Y document of particular relevance; the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such documents, such combination being obvious to a person skilled in the art.

G document member of the same patent family

Date of the actual completion of the international search

14 February 2005

Date of mailing of the international search report

10/03/2005

Name and mailing address of the ISA

European Patent Office, P.B. 5818 Patentlaan 2
NL - 2280 HV Rijswijk
Tel. (+31-70) 340-2040, Tx. 31 651 epo nl,
Fax: (+31-70) 340-3016

Authorized officer

Wagner, R

INTERNATIONAL SEARCH REPORT

International Application No
PCT/US2004/013852

C.(Continuation) DOCUMENTS CONSIDERED TO BE RELEVANT

Category *	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
E	WO 2004/071529 A (PFIZER PRODUCTS INC; COHEN, BRUCE, DAVID; BEDIAN, VAHE; WANG, HUIFEN,) 26 August 2004 (2004-08-26) page 17 - page 18	1-56
P,X	WO 03/100008 A (SCHERING CORPORATION; WANG, YAN; GREENBERG, ROBERT; PRESTA, LEONARD; P) 4 December 2003 (2003-12-04) page 69	1-56
A	HAILEY J ET AL: "NEUTRALIZING ANTI-INSULIN-LIKE GROWTH FACTOR RECEPTOR 1 ANTIBODIES INHIBIT RECEPTOR FUNCTION AND INDUCE RECEPTOR DEGRADATION IN TUMOR CELLS" MOLECULAR CANCER THERAPEUTICS, AMERICAN ASSOCIATION OF CANCER RESEARCH, US, vol. 1, no. 14, December 2002 (2002-12), pages 1349-1353, XP008026465 ISSN: 1535-7163 the whole document	1-56
A	VAUGHAN T J ET AL: "HUMAN ANTIBODIES WITH SUB-NANOMOLAR AFFINITIES ISOLATED FROM A LARGE NON-IMMUNIZED PHAGE DISPLAY LIBRARY" NATURE BIOTECHNOLOGY, NATURE PUBLISHING, US, vol. 14, 1 March 1996 (1996-03-01), pages 309-314, XP000196144 ISSN: 1087-0156 the whole document	1-56
A	WO 96/33735 A (CELL GENESYS, INC) 31 October 1996 (1996-10-31) the whole document	1-56
P,A	LU DAN ET AL: "Simultaneous blockade of both the epidermal growth factor receptor and the insulin-like growth factor receptor signaling pathways in cancer cells with a fully human recombinant bispecific antibody." JOURNAL OF BIOLOGICAL CHEMISTRY, vol. 279, no. 4, 23 January 2004 (2004-01-23), pages 2856-2865, XP002316541 ISSN: 0021-9258 the whole document	1-56

-/--

INTERNATIONAL SEARCH REPORT

International Application No

PCT/US2004/013852

C.(Continuation) DOCUMENTS CONSIDERED TO BE RELEVANT

Category *	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
------------	--	-----------------------

P, A

BURTRUM DOUGLAS ET AL: "A fully human monoclonal antibody to the insulin-like growth factor I receptor blocks ligand-dependent signaling and inhibits human tumor growth in vivo."
 CANCER RESEARCH,
 vol. 63, no. 24,
 15 December 2003 (2003-12-15), pages
 8912-8921, XP002316542
 ISSN: 0008-5472
 the whole document

1-56

INTERNATIONAL SEARCH REPORT

national application No.
PCT/US2004/013852

Box II Observations where certain claims were found unsearchable (Continuation of item 2 of first sheet)

This International Search Report has not been established in respect of certain claims under Article 17(2)(a) for the following reasons:

1. ☒ Claims Nos.:
because they relate to subject matter not required to be searched by this Authority, namely:

Although claims 34-56 are directed to a method of treatment of the human/animal body, the search has been carried out and based on the alleged effects of the compound/composition.
2. ☐ Claims Nos.:
because they relate to parts of the International Application that do not comply with the prescribed requirements to such an extent that no meaningful International Search can be carried out, specifically:
3. ☐ Claims Nos.:
because they are dependent claims and are not drafted in accordance with the second and third sentences of Rule 6.4(a).

Box III Observations where unity of invention is lacking (Continuation of item 3 of first sheet)

This International Searching Authority found multiple inventions in this international application, as follows:

1. ☐ As all required additional search fees were timely paid by the applicant, this International Search Report covers all searchable claims.
2. ☐ As all searchable claims could be searched without effort justifying an additional fee, this Authority did not invite payment of any additional fee.
3. ☐ As only some of the required additional search fees were timely paid by the applicant, this International Search Report covers only those claims for which fees were paid, specifically claims Nos.:
4. ☐ No required additional search fees were timely paid by the applicant. Consequently, this International Search Report is restricted to the invention first mentioned in the claims; it is covered by claims Nos.:

Remark on Protest

- ☐ The additional search fees were accompanied by the applicant's protest.
- ☐ No protest accompanied the payment of additional search fees.

INTERNATIONAL SEARCH REPORT

Information on patent family members

International Application No

PCT/US2004/013852

Patent document cited in search report		Publication date	Patent family member(s)	Publication date
WO 02053596	A	11-07-2002	CA 2433800 A1	11-07-2002
			CZ 20032131 A3	14-01-2004
			EE 200300318 A	15-10-2003
			EP 1399483 A2	24-03-2004
			HU 0302525 A2	28-10-2003
			JP 2004531217 T	14-10-2004
			NO 20033074 A	04-07-2003
			SK 9932003 A3	08-06-2004
			WO 02053596 A2	11-07-2002
			US 2004086503 A1	06-05-2004
			ZA 200305995 A	04-08-2004
WO 2004087756	A	14-10-2004	WO 2004087756 A2	14-10-2004
			US 2004228859 A1	18-11-2004
WO 2004083248	A	30-09-2004	WO 2004083248 A1	30-09-2004
			US 2004202655 A1	14-10-2004
WO 2004071529	A	26-08-2004	WO 2004071529 A2	26-08-2004
			US 2004202651 A1	14-10-2004
WO 03100008	A	04-12-2003	CA 2484000 A1	04-12-2003
			WO 03100008 A2	04-12-2003
			US 2004018191 A1	29-01-2004
WO 9633735	A	31-10-1996	AU 5632296 A	18-11-1996
			CA 2219361 A1	31-10-1996
			EP 0822830 A1	11-02-1998
			JP 11505523 T	21-05-1999
			WO 9633735 A1	31-10-1996
			US 6075181 A	13-06-2000
			US 6713610 B1	30-03-2004
			US 6150584 A	21-11-2000
			US 6657103 B1	02-12-2003